

## THE APPLICATION OF MOLECULAR ROTATIONAL SPECTROSCOPY TO ANALYZE REGIO- AND STEREOISOMERS OF CYCLOHEXENE PRODUCED FROM REACTIONS OF A TUNGSTEN BENZENE COMPLEX

REILLY E. SONSTROM, JATE W. BERNARD, UMME H. HOSSAIN, CHRIS A. PEDE, BROOKS PATE, JACOB A. SMITH, W. DEAN HARMAN, *Department of Chemistry, The University of Virginia, Charlottesville, VA, USA.*

Chemical reactions of transition metal complexes can provide precise stereocontrol of the products. A recent development in the Harman lab at the University of Virginia has demonstrated full control of the stereochemistry in the deuteration of benzene to cyclohexene using a benzene-tungsten metal complex. Complete stereocontrol of the deuteration is important in the development of deuterium substituted active pharmaceutical ingredients that offer improved safety through reduced metabolism. The goal of this project is to quantify any regioisomer and enantiomer impurities in one of the possible reaction products, 3-d-cyclohexene, after it has been removed from the metal and functionalized as cyclohexene oxide. Regioisomers can be identified using molecular rotational spectroscopy by simple analysis of the rotational spectrum of cyclohexene oxide. To validate that quantum chemistry provides a structure of cyclohexene oxide with sufficient accuracy to unambiguously identify all ten possible singly-deuterated isomers, these regioisomers have been identified in natural abundance in a broadband rotational spectrum (6-18 GHz) and the rotational constants compared to theoretical predictions. The more challenging analysis is the determination of the enantiomeric excess of the deuteration chemistry. The chiral tagging method is proposed for this analysis and two candidate tag molecules, propylene oxide (PO) and trifluoropropylene oxide (TFPO), have been evaluated for use in this application. Although chiral tag complexes are formed with both tags, TFPO offers two important advantages over PO. First, the signal levels for the chiral tag complex with TFPO are about a factor of four stronger – a major advantage since there is a limited amount of reaction product for testing (100 mg). Second, tagging with TFPO leads to cooling of the two ring pucker isomers of deuterated cyclohexene oxide and this simplifies the analysis of the enantiomeric composition of the sample.